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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/521,288

Applicant(s)

FLASINSKI, STANISLAW

Examiner

Ashwin Mehta

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 16-18, 23, 24 and 28-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 10-13, 16-18, 23, 24 and 28-33 is/are rejected.
- 7) ☒ Claim(s) 6-9 and 14 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 01142005: 10302006
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-14, 16, and 23 in the reply filed on November 16, 2007 is acknowledged. The traversal is on the ground(s) that the method of reducing transgene silencing can be used with a multitude of nucleotide sequences; that the disclosure gives several examples of such nucleotide sequences, such as EPSPS genes, bar genes, chloroplast transit sequences, etc. Applicant argues that the disclosure teaches several EPSPS genes from maize, rice, soybean, *Agrobacterium*, etc., and teaches subspecies for every EPSPS species, such as the artificial maize EPSPS gene modified using different codon usage tables. Applicants argue that therefore SEQ ID NOs: 3, 4, 7, 10, 17, and 18 should be considered as related species in transgenic plant (response, paragraph bridging pages 7-8). This is not found persuasive because each of SEQ ID NOs: 3, 4, 7, 10, 17, and 18 encode differing amino acid sequences, and as such make them distinct inventive concepts. Applicant also argues that the set of currently amended claims relate to a single general inventive concept, a method of reducing transgene silencing, as well as the EPSPS artificial polynucleotides employed by such method (response, page 8, 1st full paragraph). However, the nucleotide sequence of SEQ ID NO: 18 is not shared with the nucleotide sequences of any of SEQ ID NOs: 3, 7, 10, or 17. Further, all of the method claims are not limited to reducing the transgenic silencing of EPSPS genes.

Applicant has amended claims 17-18 to depend from claim 16. Claim 24 has been amended to depend from claim 23. New claims 28-33 have been introduced and ultimately depend from elected claims 1 or 10. Claims 17, 18, 24, and 28-33 will be rejoined with Group I.

Claims 17-18 and 24 will be examined only to the extent that they read on SEQ ID NOs: 26 and 27, which are subsequences of SEQ ID NO: 18. SEQ ID NOs: 24 and 25 are subsequences of non-elected SEQ ID NO: 17 are therefore not considered to be part of the elected invention.

Claims 28 and 33 will be examined to the extent that they read on SEQ ID NO: 18.

Claims 1-14, 16-18, 23, 24, 28-33, and SEQ ID NOs: 18, 26, and 27 are examined in this Office action. Non-elected subject matter should be removed from the claims. The requirement is still deemed proper and is therefore made FINAL.

Priority

2. The preliminary amendment to page 1, lines 3-4 of the specification, filed on January 14, 2005 indicates that the instant application is a national phase filing of PCT/US03/021551, which claims the benefit of priority to U.S. provisional application No. 60/396,666. However, this is incorrect. The correct U.S. provisional application number is 60/396,665.

Claim Objections

3. Claims 16-18, 23, and 24 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 16 is drawn to a DNA molecule comprising a polynucleotide molecule that specifically hybridizes to the artificial polynucleotide molecule of claim 6. Claim 23 is drawn to a DNA detection kit comprising at least one DNA molecule of sufficient length to be specifically

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homologous or complementary to the artificial polynucleotide of claim 6. Claim 6 is directed to the artificial polynucleotide molecule of SEQ ID NO: 18. Claims 16 and 23 encompass DNA molecules that are not SEQ ID NO: 18. Such molecules, including SEQ ID NOs: 26 and 27, would infringe claims 16 and 23 but not parent claim 6.

4. Claims 6-9 and 14 are objected to for encompassing non-elected inventions.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 16-18, 23, and 24 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims read on DNA molecules, or plant cells or plants, per se which can be found in nature and thus, are unpatentable to applicant. While claims 23 and 24 are directed to kits, the only recited component is the DNA molecule. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brodgers Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 10-13, and 28-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 10: the recitation, "substantially identical protein" renders the claims indefinite. The recitation, "substantially" is a relative term that has no definite meaning. The specification on page 17, lines 28-30 states, "As described herein a protein can be "substantially identical" to related proteins. These proteins with substantial identity *generally* comprise at least one polypeptide sequence that has at least ninety-eight sequence percent identity compared to its related other polypeptide sequence" (emphasis added; It is assumed that "sequence percent" should actually be --percent sequence--). However, because of the term "generally", this definition does not limit substantially identical proteins to having at least 98% sequence identity to its related other polypeptide sequence. The term "generally" does not exclude other polypeptide sequences. It is unclear what other proteins can be considered "substantially identical" to a reference protein.

Claims 1 and 29: the claims are indefinite because the last steps of the claimed methods are inconsistent with their preambles. Line 1 of both claims indicates that the methods are for reducing transgene silencing in transgenic plants. However, the last step of claim 1 yields a transgenic plant comprising an artificial polynucleotide and a known polynucleotide. The last step of claim 29 yields a transgenic plant regenerated from the plant cell of claim 10. There is no indication in either claim that transgene silencing was affected at all. The claims do not even

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indicate that the polynucleotides get expressed, or that transgene silencing occurred in the first place. It is unclear how one is to determine that transgenic silencing is reduced by the methods, if it never occurred.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 10-13, 16-18, 23, and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is broadly drawn towards a method to reduce transgene silencing in transgenic plants, comprising the steps of a) constructing an artificial polynucleotide that is divergent from a known polynucleotide that encodes a substantially identical protein; b) constructing a DNA construct comprising said artificial polynucleotide; c) transforming the construct into a plant cell, and d) regenerating a fertile transgenic plant from the plant cell, wherein the artificial polynucleotide and the known polynucleotide are less than 85% identical for their entire length and have no sequence lengths more than 23 nucleotides having 100% identity, and wherein said plant comprises both said artificial polynucleotide and the known polynucleotide. Claims 2 and 3 limit claim 1 by requiring the known polynucleotide to occur naturally in the plant or to be a

transgene, respectively. Claim 4 limits claim 1 by requiring the artificial polynucleotide is expressed in the plant. Claim 5 limits the artificial polynucleotide of the method of claim 1 to providing a phenotype selected from a recited Markush group. Claim 10 is broadly drawn to any plant cell comprising at least two polynucleotides, wherein said two polynucleotides encode substantially identical proteins and at least one of the polynucleotides is a transgene, wherein the polynucleotides are less than 85% identical for their entire length and have no sequence lengths more than 23 nucleotides having 100% identity. Claim 11 is drawn towards a plant or progeny thereof comprising the cell of claim 10. Claims 12 and 13 require the two polynucleotides of the plant or progeny of claim 11 to encode a herbicide tolerance protein. Claim 29 is broadly drawn towards a method of reducing transgene silencing in transgenic plants comprising (a) obtaining the cell of claim 10 and (b) regenerating said cell into a fertile transgenic plant. Claim 30 requires the artificial polynucleotide of the method of claim 29 to encode a herbicide tolerance protein, and claims 31 and 32 further limit the type of herbicide tolerance protein.

The Federal Circuit provided the appropriate standard for written description in University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court held that a structural description of a rat cDNA was not an adequate description of broader classes of cDNAs, because a “written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subjected matter sufficient to distinguish it from other materials.

The claimed methods and products encompass artificial polynucleotides that encode a protein that is “substantially identical” to that encoded by a known polynucleotide. As discussed

above, the discussion of "substantially identical" on pages 17-18 of the specification does not limit the level of divergence of the proteins encoded by the artificial and known polynucleotides. The specification discusses how several artificial polynucleotides encoding EPSP synthases, described in the sequence listing, were constructed, all of which were modified from a polynucleotide known to encode an EPSP synthase. Some EPSP synthases encoded by the artificial polynucleotides differ slightly from that encoded by the known or original EPSPS-encoding polynucleotide. However, no other artificial polynucleotides encoding proteins that differ from that encoded by the known or original polynucleotide are taught in the specification. The specification does not describe how other polypeptide sequences can be changed without affecting their functional activities. It is entirely unknown what amino acids are to be substituted in other polypeptides to produce other artificial polynucleotides. The example of EPSPS is not representative of any other type of protein. What criteria are used to make this determination, and what amino acids can be substituted without affecting functional activity are not described for other proteins. Given the indefiniteness of the term, "substantially identical," the protein encoded by the artificial polynucleotide doesn't even need to have the same functional activity as that encoded by the known, original polynucleotide.

Claim 16 encompasses the genus of DNA molecules comprising a polynucleotide molecule that specifically hybridizes to SEQ ID NO: 18. There is not mention in the claim of the functional activity of the hybridizing molecule or the stringency conditions of the hybridization. The claim encompasses DNA molecules that can hybridize to SEQ ID NO: 18 under any stringency condition and can have any function. Any single species of such a genus would not be representative of the remaining species, as they would have different structural and functional

properties. The only species encompassed by claim 16 that are described by the specification are SEQ ID NOs: 26 and 27.

Similarly, claim 23 encompasses a broad genus: a DNA detection kit comprising at least one DNA molecule of sufficient length to be specifically homologous or complementary to SEQ ID NO: 18, wherein the molecule is useful as a DNA probe or primer. The specification describes how such probes or primer or used to determine that the artificial polynucleotide set forth in SEQ ID NO: 18 is expressed in plants transformed with it, and to distinguish its expression from the known, unmodified polynucleotide in the plant. However, the specification only describes two species of the claimed genus: SEQ ID NOs: 26 and 27. The claim broadly encompasses DNA molecules that only need be "specifically homologous or complementary" to SEQ ID NO: 18. The specification does not define "specifically homologous", and therefore this recitation is broadly interpreted to encompass DNA molecules of any length and level of homology to SEQ ID NO: 18. The specification on page 16 states, "molecules are said to be "complementary" if they can hybridize to one another with sufficient stability to permit them to remain annealed to one another under conventional "high-stringency" conditions. Conventional stringency conditions are described by Sambrook *et al.*, 1989, and by Haymes *et al.*, *In: Nucleic Acid Hybridization, .4 Practical Approach*, IRL Press, Washington, DC (1985), herein incorporated by reference in its entirety." However, the reference to Sambrook et al. does not define the high stringency conditions. Also, essential subject matter cannot be incorporated by reference to non-patent literature. Since high stringency conditions are not defined, any level of complementarity is considered to be encompassed by claim 23. Therefore, the claimed genus encompassed widely varying species that do not share structural properties. The sequences of

SEQ ID NOs: 26 or 27 are not representative of other species encompassed by the claim. Given the breadth of the claims, the specification fails to provide an adequate written description of the multitude of artificial polynucleotides, DNA molecules hybridizing to SEQ ID NO: 18, and DNA molecules specifically homologous or complementary to SEQ ID NO: 18 encompassed by the claims.

8. Claims 1-5, 10-13, 18, and 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods, plant cells and plants wherein the artificial polynucleotide encodes the same amino acid sequence as the known polynucleotide or wherein the artificial and known polynucleotides encode an EPSPS, does not reasonably provide enablement for the claimed methods, plant cells or plants wherein the artificial and known polynucleotides encode proteins that are not identical; or plant cells or plants comprising SEQ ID NO: 26 and/or 27 but not SEQ ID NO: 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As discussed above, the specification discusses how several artificial polynucleotides encoding EPSP synthases, described in the sequence listing, were constructed, all of which were modified from a polynucleotide known to encode an EPSP synthase. Some EPSP synthases encoded by the artificial polynucleotides differ slightly from that encoded by the known or original EPSPS-encoding polynucleotide. However, the claims are not limited to artificial and known polynucleotides encoding EPSP synthases, but broadly encompass any type of proteins. The specification does not enable constructing artificial polynucleotides encoding proteins that

differ in sequence identity from that encoded by the known or original polynucleotide, except for EPSPS. No guidance is provided regarding what kind of amino acid changes can be sustained by any given protein without affecting its functional activity. The example of EPSPS is not applicable to any other type of protein, as other proteins of course have differing structures and mechanisms of action. The type of number of changes any protein can sustain, if at all, cannot be extrapolated to any other protein. In the absence of further guidance, undue experimentation would be required for one skilled in the art to determine how any given protein may be changed without affecting its functional activity.

Further, claim 18 encompasses plant cells, plants or progeny thereof comprising SEQ ID NO: 26 and/or SEQ ID NO: 27. The specification teaches that SEQ ID NOs: 26 and 27 are primers used to detect the expression of SEQ ID NO: 18 in transformed plants. However, the plant cells and plants of claim 18 do not require SEQ ID NO: 18 to be within them. No other use is taught for SEQ ID NOs: 26 or 27. The specification does not teach how one skilled in the art is to use plant cells and plants comprising SEQ ID NOs: 26 and/or 27, but not SEQ ID NO: 18. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a “mere germ of an idea does not constitute [an] enabling disclosure”, and that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention. Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4, 10, 11, 16, 23, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Drake et al. (WO 97/46690).

Claim 1 is broadly drawn towards a method to reduce transgene silencing in transgenic plants, comprising the steps of a) constructing an artificial polynucleotide that is divergent from a known polynucleotide that encodes a substantially identical protein; b) constructing a DNA construct comprising said artificial polynucleotide; c) transforming the construct into a plant cell, and d) regenerating a fertile transgenic plant from the plant cell, wherein the artificial polynucleotide and the known polynucleotide are less than 85% identical for their entire length and have no sequence lengths more than 23 nucleotides having 100% identity, and wherein said plant comprises both said artificial polynucleotide and the known polynucleotide. Claims 2 and 3 limit claim 1 by requiring the known polynucleotide to occur naturally in the plant or to be a transgene, respectively. Claim 4 limits claim 1 by requiring the artificial polynucleotide is expressed in the plant. Claim 10 is broadly drawn to any plant cell comprising at least two polynucleotides, wherein said two polynucleotides encode substantially identical proteins and at least one of the polynucleotides is a transgene, wherein the polynucleotides are less than 85% identical for their entire length and have no sequence lengths more than 23 nucleotides having 100% identity. Claim 11 is drawn towards a plant or progeny thereof comprising the cell of

claim 10. Claim 29 is broadly drawn towards a method of reducing transgene silencing in transgenic plants comprising (a) obtaining the cell of claim 10 and (b) regenerating said cell into a fertile transgenic plant.

Drake et al. teach the tomato nucleotide sequence, TOM5, encoding the phytoene synthase gene, and a modified form of that nucleotide sequence, MTOM5 (also referred to as CGS48), which encodes the same protein. TOM5 and MTOM5 have 63% sequence identity, and do not contain any lengths of more than 23 nucleotides having 100% identity. Drake et al. also teach a method to enhance expression of a selected protein in a plant having a gene that produces that protein, by transforming it with a nucleotide sequence that encodes the same protein but wherein the nucleotide sequence differs from that of the gene already present in the plant. Drake et al. assert that co-suppression occurs when plant recombinant genes are introduced into plants that already contain a gene with similar nucleotide sequence, and that co-suppression is obviated or mitigated by inserting and expressing in a plant a nucleotide sequence encoding an RNA that is different from that already present in the plant but encodes the same protein. Drake et al. provide directions for synthesizing the nucleotide sequence encoding the selected protein which differs from the natural encoding sequence. MTOM5 was inserted into a plant expression vector, operably linked to the CaMV 35S promoter, and transformed into tomato stem segments. Transformed plants were regenerated from the transformed tissue. Northern blot analysis confirmed that the MTOM5 gene sequence was expressed. With a normal GTOM5 construct, 28% of transgenic plants display a co-suppressed phenotype. All the plants carrying the modified MTOM5 construct had red fruit, demonstrating that no suppression of phytoene desaturase synthesis occurred in any of them. The transformed plants were fertile, as some were

selfed to produce progeny (pages 2-4, 7-13, claims). Claims 16 and 23 are included in this rejection because the reference teaches DNA molecules that have the inherent property of specifically hybridizing to instant SEQ ID NO: 18 under appropriate stringency conditions and/or being of sufficient length to be specifically homologous or complementary to SEQ ID NO: 18. The sentence bridging pages 15-16 of the instant application states, "As used herein, two nucleic acid molecules are said to be capable of specifically hybridizing to one another if the two molecules are capable of forming an anti-parallel, double-stranded nucleic acid structure." Any two nucleic acid molecules are capable of forming such a structure under appropriate stringency conditions.

10. Claims 16 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by New England Biolabs Catalog 1996/1997.

Claim 16 is broadly drawn to any DNA molecule comprising: any polynucleotide that specifically hybridizes to the artificial polynucleotide of claim 6 (SEQ ID NO: 18). Claim 23 is broadly drawn to a DNA detection kit comprising at least one DNA molecule of sufficient length to be specifically homologous or complementary to the artificial polynucleotide of claim 6, wherein said DNA molecule is useful as a DNA probe or DNA primer.

The New England Biolabs Catalog teaches commercially available random primers (page 111). The primers include those that inherently have the properties of specifically hybridizing to SEQ ID NO: 18 and/or being of sufficient length to be specifically homologous or complementary to SEQ ID NO: 18.

11. Claims 16, 17, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujiyama et al. (GenBank Acc. No. AG057893, 2001).

The claims are broadly drawn towards any DNA molecule comprising a polynucleotide that specifically hybridizes to SEQ ID NO: 18; or a DNA molecule comprising SEQ ID NO: 26 or SEQ ID NO: 27; or a DNA detection kit comprising at least one DNA molecule of sufficient length to be specifically homologous or complementary to SEQ ID NO: 18.

Fujiyama et al. teach a *Pan troglodytes* DNA sequence. Bases 584-569 of the reverse complement of the sequence (page 3) is the sequence set forth in instant SEQ ID NO: 26. The reference teaches a DNA molecule comprising the sequence set forth in SEQ ID NO: 26. The property of specifically hybridizing to instant SEQ ID NO: 18 under appropriate stringency conditions is inherent to the DNA molecule taught in the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-5, 10-13, 16, 23, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drake et al. (WO 97/46690) in combination with Warner et al. (WO 02/26995) and Thomas et al. (Plant J., 2001, Vol. 25, pages 417-425).

Claim 1 is broadly drawn towards a method to reduce transgene silencing in transgenic plants, comprising the steps of a) constructing an artificial polynucleotide that is divergent from a known polynucleotide that encodes a substantially identical protein; b) constructing a DNA construct comprising said artificial polynucleotide; c) transforming the construct into a plant cell, and d) regenerating a fertile transgenic plant from the plant cell, wherein the artificial polynucleotide and the known polynucleotide are less than 85% identical for their entire length and have no sequence lengths more than 23 nucleotides having 100% identity, and wherein said plant comprises both said artificial polynucleotide and the known polynucleotide. Claims 2 and 3 limit claim 1 by requiring the known polynucleotide to occur naturally in the plant or to be a transgene, respectively. Claim 4 limits claim 1 by requiring the artificial polynucleotide is expressed in the plant. Claim 5 limits the artificial polynucleotide of the method of claim 1 to providing a phenotype selected from a recited Markush group. Claim 10 is broadly drawn to any plant cell comprising at least two polynucleotides, wherein said two polynucleotides encode substantially identical proteins and at least one of the polynucleotides is a transgene, wherein the polynucleotides are less than 85% identical for their entire length and have no sequence lengths more than 23 nucleotides having 100% identity. Claim 11 is drawn towards a plant or progeny thereof comprising the cell of claim 10. Claims 12 and 13 require the two polynucleotides of the plant or progeny of claim 11 to encode a herbicide tolerance protein. Claim 29 is broadly drawn towards a method of reducing transgene silencing in transgenic plants comprising (a) obtaining the cell of claim 10 and (b) regenerating said cell into a fertile transgenic plant. Claim 30 requires the artificial polynucleotide of the method of claim 29 to encode a herbicide tolerance protein, and claims 31 and 32 further limit the type of herbicide tolerance protein.

Drake et al. is discussed above.

Drake et al. do not disclose polynucleotides encoding a herbicide tolerance protein.

Thomas et al. teach that the lower size limit required to cause post-transcriptional gene silencing of a target sequence is 23 nucleotides of complete identity (abstract; pages 418-419).

Warner et al. teach nucleotide sequences encoding glyphosate resistant EPSPS enzymes, including those from maize and soybean, and the production of glyphosate herbicide-resistant plants, comprising transforming plants with any of said nucleotide sequences (pages 18-22, 23-29, 30-31, claims).

It would have been obvious and within the scope of one of ordinary skill in the art to use the method of enhancing expression of a selected protein of Drake et al., to enhance expression of any desired protein, including one that provides the desirable trait of herbicide resistance. Drake et al. assert that co-suppression occurs when plant recombinant genes are introduced into plants that already contain a gene with similar nucleotide sequence, and that co-suppression is obviated or mitigated by inserting and expressing in a plant a nucleotide sequence encoding an RNA that is different from that already present in the plant but encodes the same protein. It would have been obvious to use the method of Drake et al. to produce an RNA that differs from an EPSPS-encoding nucleotide sequence of Warner et al., but encodes the same protein. It would have been obvious to introduce and express that modified nucleotide sequence in the transgenic plant of Warner et al. that is already expressing the unmodified EPSPS (that is, before modification by the method taught by Drake et al.), in order to achieve enhanced expression of the encoded EPSPS. That the method of modifying a nucleotide sequence encoding a selected

protein of Drake et al. produces a modified nucleotide sequence that is divergent from the original by at least 15% and has no sequence lengths of more than 23 nucleotides having 100% identity is demonstrated by the sequence MTOM5, which shares 63% identity with the unmodified TOM5 sequence. It would also have been obvious to avoid any sequence of 23 nucleotides having 100% identity in the modified nucleotide sequence, given the teaching of Thomas et al., who demonstrate that 23 nucleotides of complete sequence identity is the minimum size required to cause post-transcriptional gene silencing of a target sequence. One would have been motivated to achieve enhanced expression of EPSPS in plants, to further increase herbicide resistance of the host plant.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne Marie Grunberg, can be reached at 571-272-0975. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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/Ashwin Mehta/

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